

## SEQUENCE LISTING

| <110>   | Hara, Kenta Waterfield, Michael Yonezawa, Kazu Ludwig Institute for Cancer Research      |             |         |          |         |           |        |     |  |  |  |  |  |  |
|---|--|-------------|---------|----------|---------|-----------|--------|-----|--|--|--|--|--|--|
| <120>   | Identification and Functional Characterization of a<br>Novel Ribosomal S6 Protein Kinase |             |         |          |         |           |        |     |  |  |  |  |  |  |
| <130>   | 40750-5002-US  |             |         |          |         |           |        |     |  |  |  |  |  |  |
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|   | PCT/US99/17595<br>1999-08-04   |             |         |          |         |           |        |     |  |  |  |  |  |  |
|   | > 60/095,268<br>> 1998-08-04   |             |         |          |         |           |        |     |  |  |  |  |  |  |
| <160>   | 8  |             |         |          |         |           |        |     |  |  |  |  |  |  |
| <170>   | 170> PatentIn Ver. 2.0   |             |         |          |         |           |        |     |  |  |  |  |  |  |
| <220><221><222>   | 1816<br>DNA<br>Homo sapier<br>CDS<br>(77)(1561   | 1)          |         |          |         |           |        |     |  |  |  |  |  |  |
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| gagagagaga gagagagaga gagagagaga gagagagaga gagagagaga gagagagaga 6  gagagactcg tgccga atg gca cga ggc cga cgg gcc cgc ggc gcc 1  Met Ala Arg Gly Arg Arg Ala Arg Gly Ala Gly Ala  1 5 10 |  |             |         |          |         |           |        |     |  |  |  |  |  |  |
|   | et Ala Ala V   |             |         |          |         |           |        | 160 |  |  |  |  |  |  |
| Glu Gl  | gc gag ggc g<br>.y Glu Gly G<br>0  |             | Leu Ser |          |         |           |        | 208 |  |  |  |  |  |  |
| _   | ng ttg agg g<br>.u Leu Arg A   |             |         |          |         | _         |        | 256 |  |  |  |  |  |  |
| ata as  | og otgladt o   | rad acc add | gtg aac | att aac  | cca dad | cac atc   | aaa .  | 304 |  |  |  |  |  |  |

| Val | Glu | Leu | Thr | Glu<br>65         | Thr | Ser | Val | Asn | Val<br>70 | Gly | Pro | Glu | Arg | Ile<br>75 | Gly |     |
|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|
|     |     |     |     | gag<br>Glu        |     |     |     |     |           |     |     |     |     |           |     | 352 |
|     |     |     |     | gtg<br>Val        |     |     |     |     |           |     |     |     |     |           |     | 400 |
|     | _   | _   |     | gtc<br>Val        |     |     | _   | _   |           |     |     | _   |     | _         | _   | 448 |
|     |     |     |     | aca<br>Thr        |     |     |     |     |           |     |     |     |     |           |     | 496 |
|     |     |     |     | gtg<br>Val<br>145 |     |     |     |     |           |     |     |     |     |           |     | 544 |
|     |     |     |     | ctt<br>Leu        |     | _   |     | _   |           |     |     |     |     | _         |     | 592 |
| _   |     | _   | _   | ggc<br>Gly        |     |     |     |     |           |     |     |     |     |           |     | 640 |
| _   |     |     | _   | ctg<br>Leu        | _   | _   |     |     |           |     |     | _   |     |           |     | 688 |
|     |     | _   |     | aag<br>Lys        |     |     |     |     | _         |     | _   | _   | _   |           |     | 736 |
|     |     | _   |     | gac<br>Asp<br>225 |     |     |     | _   | -         |     |     |     |     |           |     | 784 |
| _   | _   |     |     | acc<br>Thr        |     | _   |     |     |           |     |     | _   | _   |           | _   | 832 |
|     | _   |     | _   | agt<br>Ser        |     |     |     |     | _         |     | _   |     |     | _         | _   | 880 |
|     | -   | _   | _   | tac<br>Tyr        | _   | _   |     |     |           | _   | _   |     |     |           | -   | 928 |
| gag | aac | cgg | aag | aaa               | acc | atg | gat | aag | atc       | atc | agg | ggc | aag | ctg       | gca | 976 |

| Glu Asn Arg<br>285                | Lys Lys Thr<br>290 | Met Asp Lys | Ile Ile Arg 0                         | Sly Lys Leu | Ala<br>300 |
|-----------------------------------|--------------------|-------------|---------------------------------------|-------------|------------|
| _                                 |                    |             | cgg gac ctt g<br>Arg Asp Leu V<br>310 | _           |            |
|                                   |                    |             | ggg ggt ggc c<br>Gly Gly Gly F        |             |            |
|                                   |                    |             | cgg cac atg a<br>Arg His Met A        |             | _          |
|                                   |                    | _           | ttc agg ccc t<br>Phe Arg Pro 0<br>360 |             |            |
|                                   |                    | _           | cgc ttc aca c<br>Arg Phe Thr A<br>375 |             | _          |
|                                   |                    | -           | agc gag agt g<br>Ser Glu Ser A<br>390 | _           | _          |
|                                   |                    |             | tct gtc ctg g<br>Ser Val Leu A        | _           | _          |
|                                   | _                  |             | cgc tca ccc a<br>Arg Ser Pro A<br>4   |             |            |
|                                   |                    | -           | ctc aag ttc t<br>Leu Lys Phe S<br>440 |             |            |
|                                   |                    |             | gag ccc acg g<br>Glu Pro Thr G<br>455 | lu Leu Pro  | · ·        |
|                                   |                    |             | tcg acc acc g<br>Ser Thr Thr A<br>470 |             |            |
|                                   |                    |             | tcc aag agg g<br>Ser Lys Arg G        |             |            |
| cca ggg cgc<br>Pro Gly Arg<br>495 | taggaagccg g       | gtggggtg ag | ggtagccc ttga                         | gccctg      | 1601       |

tccctgcggc tgtgagagca gcaggaccct gggccagttc cagagacctg ggggtgtgtc 1661

tgggggtggg gtgtgagtgc gtatgaaagt gtgtgtctgc tggggcagct gtgcccctga 1721
atcatgggca cggagggccg cccgccacac cccgcgctca actgctcccg tggaagatta 1781
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Glu Pro Glu Leu Ser Pro Ala Asp Ala Cys Pro Leu Ala Glu Leu Arg 35 40 45

Ala Ala Gly Leu Glu Pro Val Gly His Tyr Glu Glu Val Glu Leu Thr
50 55 60

Glu Thr Ser Val Asn Val Gly Pro Glu Arg Ile Gly Pro His Cys Phe 65 70 75 80

Glu Leu Leu Arg Val Leu Gly Lys Gly Gly Tyr Gly Lys Val Phe Gln 85 90 95

Val Arg Lys Val Gln Gly Thr Asn Leu Gly Lys Ile Tyr Ala Met Lys 100 105 110

Val Leu Arg Lys Ala Lys Ile Val Arg Asn Ala Lys Asp Thr Ala His
115 120 125

Thr Arg Ala Glu Arg Asn Ile Leu Glu Ser Val Lys His Pro Phe Ile 130 135 140

Val Glu Leu Ala Tyr Ala Phe Gln Thr Gly Gly Lys Leu Tyr Leu Ile 145 150 155 160

Leu Glu Cys Leu Ser Gly Gly Glu Leu Phe Thr His Leu Glu Arg Glu
165 170 175

Gly Ile Phe Leu Glu Asp Thr Ala Cys Phe Tyr Leu Ala Glu Ile Thr 180 185 190

Leu Ala Leu Gly His Leu His Ser Gln Gly Ile Ile Tyr Arg Asp Leu 195 200 205

- Lys Pro Glu Asn Ile Met Leu Ser Ser Gln Gly His Ile Lys Leu Thr 210 215 220
- Asp Phe Gly Leu Cys Lys Glu Ser Ile His Glu Gly Ala Val Thr His 225 230 235 240
- Thr Phe Cys Gly Thr Ile Glu Tyr Met Ala Pro Glu Ile Leu Val Arg 245 250 255
- Ser Gly His Asn Arg Ala Val Asp Trp Trp Ser Leu Gly Ala Leu Met 260 265 270
- Tyr Asp Met Leu Thr Gly Ser Pro Pro Phe Thr Ala Glu Asn Arg Lys 275 280 285
- Lys Thr Met Asp Lys Ile Ile Arg Gly Lys Leu Ala Leu Pro Pro Tyr 290 295 300
- Leu Thr Pro Asp Ala Arg Asp Leu Val Lys Lys Phe Leu Lys Arg Asn 305 310 315 320
- Pro Ser Gln Arg Ile Gly Gly Gly Pro Gly Asp Ala Ala Asp Val Gln 325 330 335
- Arg His Pro Phe Phe Arg His Met Asn Trp Asp Asp Leu Leu Ala Trp 340 345 350
- Arg Val Asp Pro Pro Phe Arg Pro Cys Leu Gln Ser Glu Glu Asp Val 355 360 365
- Ser Gln Phe Asp Thr Arg Phe Thr Arg Gln Thr Pro Val Asp Ser Pro 370 375 380
- Asp Asp Thr Ala Leu Ser Glu Ser Ala Asn Gln Ala Phe Leu Gly Phe 385 390 395 400
- Thr Tyr Val Ala Pro Ser Val Leu Asp Ser Ile Lys Glu Gly Phe Ser 405 410 415
- Phe Gln Pro Lys Leu Arg Ser Pro Arg Arg Leu Asn Ser Ser Pro Arg
  420 425 430
- Val Pro Val Ser Pro Leu Lys Phe Ser Pro Phe Glu Gly Phe Arg Pro 435 440 445
- Ser Pro Ser Leu Pro Glu Pro Thr Glu Leu Pro Leu Pro Pro Leu Leu 450 , 455 460
- Pro Pro Pro Pro Pro Ser Thr Thr Ala Pro Leu Pro Ile Arg Pro Pro 465 470 475 480
- Ser Gly Thr Lys Lys Ser Lys Arg Gly Arg Gly Arg Pro Gly Arg 485 490 495

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ttt tac cca gcc ccg gac ttc cga gac agg gaa gct gag gac atg gca
                                                                   102
Phe Tyr Pro Ala Pro Asp Phe Arg Asp Arg Glu Ala Glu Asp Met Ala
                                         20
                     15
                                                                   150
gga gtg ttt gac ata gac ctg gac cag cca gag gac gcg ggc tct gag
Gly Val Phe Asp Ile Asp Leu Asp Gln Pro Glu Asp Ala Gly Ser Glu
gat gag ctg gag gag ggt cag tta aat gaa agc atg gac cat ggg
                                                                   198
Asp Glu Leu Glu Glu Gly Gly Gln Leu Asn Glu Ser Met Asp His Gly
gga gtt gga cca tat gaa ctt ggc atg gaa cat tgt gag aaa ttt gaa
                                                                   246
Gly Val Gly Pro Tyr Glu Leu Gly Met Glu His Cys Glu Lys Phe Glu
                             65
atc tca gaa act agt gtg aac aga ggg cca gaa aaa atc aga cca gaa
                                                                   294
Ile Ser Glu Thr Ser Val Asn Arg Gly Pro Glu Lys Ile Arg Pro Glu
tgt ttt gag cta ctt cgg gta ctt ggt aaa ggg ggc tat gga aag gtt
                                                                   342
Cys Phe Glu Leu Arg Val Leu Gly Lys Gly Tyr Gly Lys Val
ttt caa gta cga aaa gta aca gga gca aat act ggg aaa ata ttt gcc
                                                                   390
Phe Gln Val Arg Lys Val Thr Gly Ala Asn Thr Gly Lys Ile Phe Ala
                110
                                    115
atg aag gtg ctt aaa aag gca atg ata gta aga aat gct aaa gat aca
                                                                   438
Met Lys Val Leu Lys Lys Ala Met Ile Val Arg Asn Ala Lys Asp Thr
                                130
            125
get cat aca aaa gea gaa egg aat att etg gag gaa gta aag eat eee
                                                                   486
Ala His Thr Lys Ala Glu Arg Asn Ile Leu Glu Glu Val Lys His Pro
        140
                            145
ttc atc gtg gat tta att tat gcc ttt cag act ggt gga aaa ctc tac
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Phe Ile Val Asp Leu Ile Tyr Ala Phe Gln Thr Gly Gly Lys Leu Tyr
    155
                        160
                                            165
ctc atc ctt gag tat ctc agt gga gga gaa cta ttt atg cag tta gaa
                                                                   582
Leu Ile Leu Glu Tyr Leu Ser Gly Gly Glu Leu Phe Met Gln Leu Glu
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180 185 170 175 aga gag gga ata ttt atg gaa gac act gcc tgc ttt tac ttg gca gaa Arg Glu Gly Ile Phe Met Glu Asp Thr Ala Cys Phe Tyr Leu Ala Glu atc tcc atg gct ttg ggg cat tta cat caa aag ggg atc atc tac aga 678 Ile Ser Met Ala Leu Gly His Leu His Gln Lys Gly Ile Ile Tyr Arg 210 726 gac ctg aag ccg gag aat atc atg ctt aat cac caa ggt cat gtg aaa Asp Leu Lys Pro Glu Asn Ile Met Leu Asn His Gln Gly His Val Lys 220 225 cta aca gac ttt gga cta tgc aaa gaa tct att cat gat gga aca gtc 774 Leu Thr Asp Phe Gly Leu Cys Lys Glu Ser Ile His Asp Gly Thr Val 235 aca cac aca ttt tgt gga aca ata gaa tac atg gcc cct gaa atc ttg 822 Thr His Thr Phe Cys Gly Thr Ile Glu Tyr Met Ala Pro Glu Ile Leu 250 255 atq aqa aqt qqc cac aat cgt gct gtg gat tgg tgg agt ttg gga gca 870 Met Arg Ser Gly His Asn Arg Ala Val Asp Trp Trp Ser Leu Gly Ala 270 tta atg tat gac atg ctg act gga gca ccc cca ttc act ggg gag aat 918 Leu Met Tyr Asp Met Leu Thr Gly Ala Pro Pro Phe Thr Gly Glu Asn 285 aga aag aaa aca att gac aaa atc ctc aaa tgt aaa ctc aat ttg cct 966 Arg Lys Lys Thr Ile Asp Lys Ile Leu Lys Cys Lys Leu Asn Leu Pro 300 305 ccc tac ctc aca caa gaa gcc aga gat ctg ctt aaa aag ctg ctg aaa 1014 Pro Tyr Leu Thr Gln Glu Ala Arg Asp Leu Leu Lys Lys Leu Leu Lys 315 320 aga aat get get tet egt etg gga get ggt eet ggg gae get gga gaa 1062 Arg Asn Ala Ala Ser Arg Leu Gly Ala Gly Pro Gly Asp Ala Gly Glu 330 335 340 gtt caa gct cat cca ttc ttt aga cac att aac tgg gaa gaa ctt ctg 1110 Val Gln Ala His Pro Phe Phe Arg His Ile Asn Trp Glu Glu Leu Leu 350 360 355 gct cga aag gtg gag ccc ccc ttt aaa cct ctg ttg caa tct gaa gag 1158 Ala Arg Lys Val Glu Pro Pro Phe Lys Pro Leu Leu Gln Ser Glu Glu 365 375 gat gta agt cag ttt gat tcc aag ttt aca cgt cag aca cct gtc gac 1206 Asp Val Ser Gln Phe Asp Ser Lys Phe Thr Arg Gln Thr Pro Val Asp 380 385 age cca gat gac tca act ctc agt gaa agt gcc aat cag gtc ttt ctg 1254

Ser Pro Asp Asp Ser Thr Leu Ser Glu Ser Ala Asn Gln Val Phe Leu

|      | 395        |       |                   |       |       | 400   |       |       |       |       | 405  |       |       |                   |        |      |
|------|------------|-------|-------------------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------------------|--------|------|
|      |            |       |                   | _     |       |       |       | _     |       | -     |      | -     |       | gaa<br>Glu        |        | 1302 |
|      |            |       | _                 |       |       |       | _     |       |       | _     | _    |       |       | ggc<br>Gly<br>440 | _      | 1350 |
|      | -          |       |                   |       |       |       |       |       |       |       |      |       |       | ttc<br>Phe        |        | 1398 |
|      | _          |       | _                 | _     | _     | _     |       | _     |       |       | _    |       |       | gtg<br>Val        | _      | 1446 |
|      |            |       |                   |       |       |       |       |       |       |       |      |       |       | atg<br>Met        |        | 1494 |
|      | _          | _     | _                 | _     |       |       |       |       | _     | _     | _    |       |       | gly<br>ggg        |        | 1542 |
|      |            |       |                   | _     |       |       | _     |       |       |       |      |       |       | cac<br>His<br>520 | _      | 1590 |
| _    | atg<br>Met |       | cta<br>Leu<br>525 | tgad  | agag  | gca a | atgct | ttta  | aa to | gaatt | taag | g gca | aaaa  | aggt              |        | 1642 |
| ggag | gaggg      | gag a | atgto             | gtgag | gc at | ccto  | gcaaç | ggtg  | gaaac | caag  | acto | caaaa | atg . | acagt             | ttcag  | 1702 |
| agag | jtcaa      | atg 1 | catt              | acat  | a ga  | acac  | cttcg | ggad  | cacaç | ggaa  | aaat | caaa  | gt    | ggatt             | ttaaa  | 1762 |
| aaat | caat       | ca a  | atggt             | gcaa  | aa aa | aaaa  | actta | a aag | gcaaa | aata  | gtat | tgct  | ga    | actct             | taggc  | 1822 |
| acat | caat       | ta a  | attga             | attco | et co | gcgad | catct | tto   | ctcaa | acct  | tato | caago | gat   | tttca             | atgttg | 1882 |
| atga | ctc        | gaa a | actga             | acagt | a tt  | aagg  | ggtag | g gat | gtt   | gctc  | tgaa | atcad | etg   | tgagt             | ctgat  | 1942 |
| gtgt | gaag       | gaa q | gggta             | atcct | t to  | catta | aggca | a agt | acaa  | aatt  | gcct | tataa | ata   | cttgo             | caacta | 2002 |
| agga | caaa       | att a | agcat             | gcaa  | ag ct | tggt  | caaa  | a ctt | ttco  | ccag  | gcaa | aaatg | 199   | aaggo             | caaaga | 2062 |
| caaa | agaa       | aac t | taco              | caatt | g at  | gttt  | tace  | g tgo | caaac | caac  | ctga | aatct | tt    | tttt              | atata  | 2122 |
| aata | tata       | att 1 | ttca              | aaata | ag at | tttt  | gatt  | cag   | gctca | atta  | tgaa | aaaa  | cat   | cccaa             | acttt  | 2182 |
| aaaa | tgcg       | gaa a | attat             | tggt  | t gg  | gtgtg | gaaga | a aag | gccag | gaca  | actt | ctgt  | tt    | cttct             | cttgg  | 2242 |
| tgaa | ataa       | ata a | aaato             | caaa  | at da | atca  | attat | taa   | acaca | aget  | atac | acto  | att   | taaa              | gatta  | 2302 |

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<213> Homo sapiens

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20 25 30

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Gln Leu Asn Glu Ser Met Asp His Gly Gly Val Gly Pro Tyr Glu Leu 50 55 60

Gly Met Glu His Cys Glu Lys Phe Glu Ile Ser Glu Thr Ser Val Asn 65 70 75 80

Arg Gly Pro Glu Lys Ile Arg Pro Glu Cys Phe Glu Leu Leu Arg Val 85 90 95

Leu Gly Lys Gly Gly Tyr Gly Lys Val Phe Gln Val Arg Lys Val Thr
100 105 110

Gly Ala Asn Thr Gly Lys Ile Phe Ala Met Lys Val Leu Lys Lys Ala 115 120 125

Met Ile Val Arg Asn Ala Lys Asp Thr Ala His Thr Lys Ala Glu Arg 130 135 140

Asn Ile Leu Glu Glu Val Lys His Pro Phe Ile Val Asp Leu Ile Tyr 145 150 155 160

Ala Phe Gln Thr Gly Gly Lys Leu Tyr Leu Ile Leu Glu Tyr Leu Ser 165 170 175

Gly Glu Leu Phe Met Gln Leu Glu Arg Glu Gly Ile Phe Met Glu 180 185 190

Asp Thr Ala Cys Phe Tyr Leu Ala Glu Ile Ser Met Ala Leu Gly His 195 200 205

Leu His Gln Lys Gly Ile Ile Tyr Arg Asp Leu Lys Pro Glu Asn Ile 210 215 220

Met Leu Asn His Gln Gly His Val Lys Leu Thr Asp Phe Gly Leu Cys 225 230 235 240

Lys Glu Ser Ile His Asp Gly Thr Val Thr His Thr Phe Cys Gly Thr Ile Glu Tyr Met Ala Pro Glu Ile Leu Met Arg Ser Gly His Asn Arg Ala Val Asp Trp Trp Ser Leu Gly Ala Leu Met Tyr Asp Met Leu Thr Gly Ala Pro Pro Phe Thr Gly Glu Asn Arg Lys Lys Thr Ile Asp Lys Ile Leu Lys Cys Lys Leu Asn Leu Pro Pro Tyr Leu Thr Gln Glu Ala Arg Asp Leu Leu Lys Leu Leu Lys Arg Asn Ala Ala Ser Arg Leu Gly Ala Gly Pro Gly Asp Ala Gly Glu Val Gln Ala His Pro Phe Phe

Arg His Ile Asn Trp Glu Glu Leu Leu Ala Arg Lys Val Glu Pro Pro

Phe Lys Pro Leu Gln Ser Glu Glu Asp Val Ser Gln Phe Asp Ser 

Lys Phe Thr Arg Gln Thr Pro Val Asp Ser Pro Asp Asp Ser Thr Leu 

Ser Glu Ser Ala Asn Gln Val Phe Leu Gly Phe Thr Tyr Val Ala Pro 

Ser Val Leu Glu Ser Val Lys Glu Lys Phe Ser Phe Glu Pro Lys Ile 

Arg Ser Pro Arg Arg Phe Ile Gly Ser Pro Arg Thr Pro Val Ser Pro 

Val Lys Phe Ser Pro Gly Asp Phe Trp Gly Arg Gly Ala Ser Ala Ser 

Thr Ala Asn Pro Gln Thr Pro Val Glu Tyr Pro Met Glu Thr Ser Gly 

Ile Glu Gln Met Asp Val Thr Met Ser Gly Glu Ala Ser Ala Pro Leu 

Pro Ile Arg Gln Pro Asn Ser Gly Pro Tyr Lys Lys Gln Ala Phe Pro 

Met Ile Ser Lys Arg Pro Glu His Leu Arg Met Asn Leu 

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             20
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Ser Gln Lys
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<213> Artificial Sequence
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                  5
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<213> Artificial Sequence
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## isoforms

Gln Lys